The Inhibition by Guinea Pig Serum of the Growth of the Murphy-Sturm Lymphosarcoma*

ELOISE JAMESON, HERMAN AINIS,† AND R. MARK RYAN

(University of Southern California, Department of Medicine, Los Angeles, Calif.)

Kidd (7) showed that there is a spectrum of inhibitory activity of guinea pig serum against lymphomas transplanted in rats and mice.

Experiments previously reported from our laboratory (Jameson et al. [6]) demonstrated that guinea pig serum was effective in delaying the onset and slowing the growth of the ACMCA2 fibrosarcoma when carried in the AXC 9935 strain of the Irish gray rat. This tumor had no spontaneous regressions in the host.

This work was extended to study the effect of guinea pig serum against the Murphy-Sturm lymphosarcoma, which was reported to have 20 per cent spontaneous regressions (Dunham and Stewart [3]).

MATERIALS AND METHODS

The Murphy-Sturm lymphosarcoma1 was acquired as an ascites tumor and was transformed to the solid state by subcutaneous implantation. The tumor was carried in Wistar2 strain albino rats. In total, 130 control animals and 143 experimental animals were used in a series of seven experiments with the solid tumor. Each group implanted with the ascites tumor contained fifteen animals.

Transplantation.—The solid tumor was transplanted subcutaneously into the back, in a 1 per cent suspension of cells obtained by employing Bernfeld and Homburger's (1) modification of Snell's cytosieve procedure.

The cells from the ascites tumor were collected in sodium citrate which was made up to a final concentration of 0.5 per cent of the salt. The cell suspension was freed from erythrocytes by the procedure of differential lysis as described by Hoecker and Hauschka (4). The suspension was adjusted to a final concentration of 100 million cells/ml with Snell's (8) buffered glucose Ringer's solution; 0.2 ml. was injected intraperitoneally into each rat.

Guinea pig serum.—The guinea pig serum was obtained aseptically from a heterogeneous colony of guinea pigs; 1,000 units of penicillin G (potassium)3 were added per ml. of serum. The serum was tested for contamination, and only sterile serum was employed in the experiments. The serum was stored at −20° C. until needed.

Treatment.—Intraperitoneal injections of 3 ml. of guinea pig serum were initiated immediately after the tumor was implanted. The animals implanted subcutaneously were given three series of three daily injections, separated by 3 days of rest. This schedule had been found most effective against the ACMCA2 fibrosarcoma (Jameson et al. [5]). The animals implanted with ascites tumors were given one series of three daily injections.

Tumor detection.—The animals were examined daily for the appearance of palpable tumors or abdominal distention.

Results obtained from the experiments with the solid tumor varied appreciably. In some experiments guinea pig serum was very effective against the tumors; in others, only a slight inhibition was observed. An examination of the data indicated that guinea pig serum was less effective in those experiments in which the tumors started appearing very early in the control animals and was more effective when there was a longer latent period in the controls. The experiments were therefore arbitrarily divided into two groups on the basis of the latent period. One group consisted of four experiments in which palpable tumors started appearing very early in the control animals and was more effective when there was a longer latent period in the controls. The experiments were therefore divided into two groups on the basis of the latent period. One group consisted of four experiments in which palpable tumors started appearing in the control animals in less than 5 days. This group contained 71 controls and 100 experimental animals. The second group included 59 controls and 43 experimental animals from the three experiments in which the control animals did not

* Supported in part by Mr. and Mrs. John J. Elmore and the University of Southern California, Department of Medicine. We are indebted to the Hancock Foundation for laboratory space and facilities.

† Present address: Department of Chemistry, California Institute of Technology, Pasadena, California.

1 Obtained from Dr. D. Simonson, City of Hope Medical Center, Duarte, Calif.

2 Obtained from Pacific Animal Farms, Los Angeles, Calif.

Received for publication April 11, 1958.
demonstrate palpable tumors until at least 5 days after implanting.

Influence of the donor tumor.—To determine whether the donor tumor had any effect on the fate of the transplanted tumor, the age and size of the donor tumors were compared with the latent period and the number of regressions of the transplanted tumors.

RESULTS

Subcutaneous tumor.—Chart 1 shows the two groups of controls and the effect of guinea pig serum on each treated group. In the control groups

<table>
<thead>
<tr>
<th>Days After Implanting</th>
<th>PER CENT. OF ANIMALS WITH PALPABLE TUMORS</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>5</td>
<td>0</td>
</tr>
<tr>
<td>10</td>
<td>0</td>
</tr>
<tr>
<td>15</td>
<td>0</td>
</tr>
<tr>
<td>20</td>
<td>0</td>
</tr>
<tr>
<td>25</td>
<td>0</td>
</tr>
<tr>
<td>30</td>
<td>0</td>
</tr>
<tr>
<td>35</td>
<td>0</td>
</tr>
<tr>
<td>40</td>
<td>0</td>
</tr>
<tr>
<td>45</td>
<td>0</td>
</tr>
<tr>
<td>50</td>
<td>0</td>
</tr>
</tbody>
</table>

in which the tumors were first palpable in less than 5 days, all the tumors appeared within a 3-day period; whereas in the control groups in which tumors did not first appear until 5 days after implantaing, it required a 10-day period before all the tumors had appeared.

When guinea pig serum was injected into the animals in these two groups, the results were quite different. In both cases the guinea pig serum was obviously effective. In both groups there was a definite prolongation of the latent period, not only in the time before the tumors first became detectable, but in the time of appearance of subsequent tumors as well, producing a more extended latent period. In addition to this, it can be noted that in the two control groups 100 per cent and 97 per cent of the tumors appeared; however, in the two treated groups only 87 per cent and 42 per cent of the tumors appeared during the 50 days the animals were observed.

Treatment with guinea pig serum was effective in inhibiting the tumors completely in a large number of animals of both treated groups. This effect was more pronounced in the group with a latent period of at least 5 days. In this group, too, the number of regressions was increased to 83 per cent as compared with 55 to 56 per cent in the other three groups.

No correlation could be found between either the size or age of the donor tumor and the latent period or number of spontaneous regressions in the transplanted tumor.

DisCUSSION

It appears that the effectiveness of guinea pig serum in inhibiting the solid form of the Murphy-Sturm lymphosarcoma is dependent, in part at least, on the time necessary for the tumor to establish itself.

It is not known what factors control the difference in the latent period in the various tumors.
Bruwer et al. (2) indicated that there is a relationship between the age of the tumor and its subsequent fate when transplanted. On the basis of our several experiments, neither the latent period nor the number of regressions could be correlated with the age or size of the donor tumor.

Kidd (7) reported that guinea pig serum acted only in lengthening the latent period of this lymphosarcoma. The fact that a more effective inhibition is demonstrated in our experiments may be explained by the different sub-lines of the tumor and rats that were used, resulting in different tumor-host relationships. The importance of these differences is apparent when the greater number of spontaneous regressions which we observed in our experiments is compared with those reported in the literature. It is also possible that the tumor Kidd used was in a state comparable to that of those tumors with which we observed a short latent period and subsequent increased resistance to treatment with guinea pig serum.

The ascites form of this tumor is fatal in one-half to one-third the time required for the solid tumor to kill its host. That guinea pig serum is effective in inhibiting the ascites form suggests that the latent period serves to permit a sufficient accumulation of guinea pig serum at the tumor site. In the ascites form, the tumor cells are bathed directly in the guinea pig serum injected.

Kidd suggested that guinea pig serum acts, in part, directly on the tumor cells and alters them so that they become more susceptible to the defensive mechanisms of the host. This opinion is supported by the action of guinea pig serum on the ascites tumor and also by its increased effectiveness when there is a longer latent period in the development of the solid tumor.

**SUMMARY**

Intraperitoneal injections of guinea pig serum are more effective in inhibiting growth of the solid form of the Murphy-Sturm lymphosarcoma carried in Wistar rats when there is a latent period of at least 5 days. Disparities between two groups of animals that have shorter and longer latent periods, respectively, are manifested by differences in: (a) the number of tumors that are completely inhibited, (b) the length of the latent period, and/or (c) the number of tumor regressions.

Intraperitoneal injections of guinea pig serum are shown to be effective in inhibiting growth of the more virulent ascites form of this tumor.

**REFERENCES**

The Inhibition by Guinea Pig Serum of the Growth of the Murphy-Sturm Lymphosarcoma

Eloise Jameson, Herman Ainis and R. Mark Ryan


Updated version
Access the most recent version of this article at:
http://cancerres.aacrjournals.org/content/18/7/866

E-mail alerts
Sign up to receive free email-alerts related to this article or journal.

Reprints and Subscriptions
To order reprints of this article or to subscribe to the journal, contact the AACR Publications Department at pubs@aacr.org.

Permissions
To request permission to re-use all or part of this article, contact the AACR Publications Department at permissions@aacr.org.